

Roberto Angelo MOTTERLINI
Appl. No. 10/535,508
Atty. Ref.: 620-371
Amendment
April 1, 2008

REMARKS

Reconsideration is requested.

Claims 2 and 11-15 have been canceled, without prejudice. Claims 16-23 have been added. Claims 1, 3-10 and 16-23 are pending. Support for the revisions to claim 1 may be found, for example, in on page 3, lines 13-14 and page 3, lines 14-16. Support for the additional recitations of claim 16 may be found, for example, in page 12, lines 3-6 of the specification. Claims 17-23 find support throughout the specification and, for example, claims 3 and 6-10. No new matter has been added.

Return of an initialed copy of the attached PTO/SB/08a Form as confirmation of the Examiner's consideration of the listed documents and information is requested. The requisite fee for consideration of the documents and information is attached. The undersigned further notes that the Examiner of co-pending application no. 11/275,780 has provisionally rejected claims 1-10 and 12 of the co-pending application under the judicially created doctrine of obviousness-type double patenting over claims 1-15 and 23-25 of copending application Serial No. 10/535,226. The Examiner of co-pending application no. 11/275,780 has provisionally rejected claims 1-10 and 12 of the co-pending application under the judicially created doctrine of obviousness-type double patenting over claims 1-15 of the present application no. 10/535,508 is traversed. The Examiner of co-pending application no. 11/275,780 has provisionally rejected claims 1-10 and 12 under the judicially created doctrine of obviousness-type double patenting over claims 1-32 of copending application Serial No. 10/567,157. The publications listed in the attached PTO/SB/08a Form are U.S. Patent Office publications of the noted

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co-pending applications and the attached and listed claims are copies of the pending claims. Return of an initialed copy of the attached PTO/SB/08a Form is requested.

A Terminal Disclaimer over Application No. 11/275,780, is being filed herewith, without prejudice.

The Section 102 rejection of claims 1-4 and 6-9 over Motterlini (Carbon Monoxide-releasing Molecules Characterization of Biochemical and Vascular Activities, Circulation Research, published 02/08/2002), is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following distinguishing comments.

This document describes experiments to examine the effects of carbon monoxide-releasing molecules (CO-RMs) on mitigation of vasoconstriction. It describes an investigation of the effects of tricarbonyldichlororuthenium (II) dimer ($[\text{Ru}(\text{CO})_3\text{Cl}_2]_2$) on isolated aortic rings and dimanganese decacarbonyl ($[\text{Mn}_2(\text{CO})_{10}]$) on isolated rat hearts from male Lewis rats (see page 21 of the document).

The experiments reported in the cited art involved test tissue isolated from the living animals, in order to provide reproducibility, and ease of experimental procedure. The methods of the cited art however do not literally or inherently involve donated transplantation organs or isolated organs according to the claimed invention.

Rather, the conclusion of Motterlini et al is that:

"In the long term, transition metal carbonyls could be utilized for the therapeutic delivery of CO to alleviate vascular- and immuno-related dysfunction." See Abstract, penultimate sentence.

Motterlini et al. does not literally or inherently teach a method of the claims involving 'isolated' organs as defined in the claims. The organs of the cited art are removed from the rats, suspended in an organ bath containing oxygenated Krebs-Henseleit buffer and tested for relaxation response to cumulative doses of the test compound. See page 19, Materials and Methods of the cited document. The test materials were presumably discarded after testing. These methods do not constitute contacting an active compound with an isolated organ or an extracorporeal organ according to the claimed invention.

As the cited art fails to teach each and every aspect of the claimed invention, the Section 102 rejection of the claims should be withdrawn.

For completeness, the applicants note that the claimed method limits post-ischaemic damage to the organs of the claims.

Motterlini et al. relates to studies on vasodilatory effects of metal carbonyls. Hypertension, which can be caused by vasoconstriction, is a different disease state to post-ischaemic organ damage. Ischaemia is the damage that results to an organ from O₂ deprivation caused by a reduction in blood supply. In the method of the present application, the organ to be treated is isolated from blood supply, so there is no blood flow. The organ may be already considered to be ischaemic. Reperfusion of organs with oxygenated blood during transplant procedures results in damage to the organ, which is referred to in the medical field as post-ischaemic damage.

The methods of the present application relate to limiting damage to an ischaemic organ when the blood supply has been restored (i.e. post-ischaemia). The method of

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the invention therefore relates to the treatment of reperfusion injury. The invention involves treatment of the 'isolated' organ or the donated transplantation organ in order to reduce or limit post-ischaemic damage when the organ is subsequently restored to a blood supply.

Motterlini does not involve the effects of post-ischaemic damage as, for example, the heart (and aorta ring sections) are used purely for research purposes, and are not replaced in the body. The blood supply is not reconnected to the organs, such that the possibility of post-ischaemic damage does not arise.

The claims are patentable over the cited art and withdrawal of the Section 102 rejection based on Motterlini is requested.

The Section 102 rejection of claims 1-3 and 5-11 over Clark (Cardioprotective Actions by Water-Soluble Carbon Monoxide-Releasing Molecular, Circulation Research, published 07/25/2003), is traversed. Reconsideration and withdrawal of the rejection are requested as the document was published after the applicants claimed priority date of November 20, 2002. A certified copy of the priority application has been filed and the claims are believed to be supported by the priority application. Withdrawal of the Section 102 rejection is requested. The Examiner is requested to contact the undersigned in the event anything further is required in this regard.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned in the event anything further is required in this regard.

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Respectfully submitted,

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